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EXAMINER	
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ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,944	GRAY ET AL.	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,46,56-58,61 and 133* is/are rejected.

7)☒ Claim(s) *1,46,56,57 and 133* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/04/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *SEQ ALIGN*.

Continuation of Disposition of Claims: Claims pending in the application are 1,46,56-58,61,64,66,68,70,73,125,126,130,131,133,135,137,138,140,157,161,169,171,218,221,225,229,231-234,236,241 and 271-273.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 64,66,68,70,73,125,126,130,131,135,137,138,140,157,161,169,171,218,221,225,229,231-234,236,241 and 271-273.

Detailed Action

Claims 1, 46, 56-58, 61, 64, 66, 68, 70, 73, 125, 126, 130, 131, 133, 135, 137, 138, 140, 157, 161, 169, 171, 218, 221, 225, 229, 231-234, 236, 241 and 271-273 are pending in this application for examination. Claims 1, 46, 56-58, 61 and 133 in part are now under consideration. Claims 64, 66, 68, 70, 73, 125, 126, 130, 131, 135, 137, 138, 140, 157, 161, 169, 171, 218, 221, 225, 229, 231-234, 236, 241 and 271-273 are withdrawn as they are drawn to non-elected invention.

Election/Restrictions

Applicants' election of Group I, claims 1, 46, 56-58, 61 and 133 with respect to a polynucleotide sequence of SEQ ID NO: 7 encoding a polypeptide of sequence of SEQ ID NO: 8 with traverse for prosecution in the reply filed on 04/25/08 is acknowledged. The traversal is on the grounds that following the entry of amendments, the claims will be linked so as to form a general inventive concept and therefore unity of invention exists between the restricted groups (Groups II to XXII) and the elected Group I, as all the claims are closely related and also possess novel inventive concept and examination of all the claims will not pose a serious search burden.

Applicants arguments of "unity of invention exists between the restricted groups (Groups II to XXII) with the elected Group I, as all the claims are closely related and also possess novel inventive concept and examination of all the claims will not pose a serious search burden" is answered as follows.

Applicant's argument of all the claims are linked by special technical features and have unity of invention is not persuasive, because Hulsmann et al., (J. Bacteriol., 2000, Vol. 182 (22): 6292-6301 and see provided sequence alignments) teach the isolation of a polynucleotide with 100% homology to the polynucleotide of SEQ ID NO: 7 of the instant application (claims 1 (a)-

(c) and (e)-(i), 46, 56, 57 and claims 58 and 61 in part), said reference polynucleotide encodes for six genes including an open reading frame annotated as alpha-gluocosidase that hydrolyzes glucosidic bonds; 1, 4-α-D-glucan glucohydrolase activity, said reference polypeptide has 93.1% sequence homology and a 100% best local similarity to SEQ ID NO: 8 or enzymatically active fragment thereof of the instant application (claim 1(d)). Therefore the technical features linking the inventions of Groups I-XXII does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. Further evidence that the claims lack special technical feature is found under U.S.C. 102 (b) rejection below. In addition, as cited in the Office action dated 01/18/08 (Requirement for Restriction), the PCT does not provide for multiple products or methods within single application, therefore, unity of invention is lacking with regard to Groups I-XXII; see 37 CFR 1.475. 37 CFR 1.475 (d) also states: If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) 1.47(c).

Therefore, for the above cited reasons searching of all claims is a serious search burden and contrary to applicant's argument, the requirement is still deemed proper and is therefore made FINAL.

Priority

Acknowledgment is made of applicants' claim for priority under 35 U.S.C. 371 to PCT International Application Serial No: PCT/US03/33150 filed on 10/15/2003, which claims benefit of the U.S. Provisional application (USSN) 60/423,626 filed on 10/31/2002.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 08/04/2005 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the IDS is considered by the examiner.

Objections to Abstract

The Abstract of the disclosure is objected to because, Abstract should be on a separate sheet of paper. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claims 1, 46, 56, 57 and 133 are objected to, due to the following informalities:

Claim 1 is replete with typographical errors wherein the assignments for sub-parts for the claim are incorrect. Examiner has endeavored to identify the errors, however, for consistency sake applicants' are urged to carefully scrutinize the claim and amend the claim appropriately.

Claim 1, page 3, line 18 recites "(d)", typographical error, should read as "(f)" as there is already part "(d)" on line 4.

Claim 1, page 3, line 20 recites "(e) the nucleic acid of any of (a) to (d)", typographical error, should read as "(g) the nucleic acid of any of (a) to (f)".

Claim 1, page 4, line 1 recites "(f) the nucleic acid of any of (a) to (e)", typographical error, should read as "(h) the nucleic acid of any of (a) to (g)".

Claim 1, page 4, line 3 recites "(g) the nucleic acid of any of (a) to (f)", typographical error, should read as "(i) the nucleic acid of any of (a) to (h)".

Claim 1, page 4, line 5 recites "(h) the nucleic acid of (g)", typographical error, should read as "(j) the nucleic acid of (i)".

Claim 1, page 4, line 7 recites "(i) the nucleic acid sequence fully complementary to any of (a) to h)", typographical error, should read as "(k) the nucleic acid sequence fully complementary to any of (a) to (j)".

Claim 1 (d) is objected to, because the claim as written, it is not clear to the examiner whether a nucleic acid sequence encoding a polypeptide having the sequence of SEQ D NO: 8 or enzymatically active fragments thereof has amylase activity or any enzymatic activity. For examination purposes the polypeptide of SEQ ID NO: 8 is deemed to have amylase activity (1, 4-α-D-glucan glucohydrolase activity).

Claim 1 (e) typographical error, 1,4-α-D-glucan glucohydralase activity is spelt incorrectly, should read as 1,4-α-D-glucan glucohydrolase activity.

Claim 46, typographical error, said claim recites "Claims 46", amend the claim to recite "Claim 46".

Claim 56, as written is grammatically awkward, examiner suggests amending the claim as follows "An expression cassette comprising the nucleic acid sequence of claim 1". Appropriate correction is required.

Claim 57, as written is grammatically awkward; examiner suggests amending the claim as follows "A vector comprising the nucleic acid sequence of claim 1". Appropriate correction is required.

Claim 133 contains non-elected subject matter such as immobilized polypeptide (depending from non-elected claim 73), the heterodimer (depending from non-elected claim 126), the antibody (depending from non-elected claim 135). Appropriate correction is required.

Claim Rejections: 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1, 46, 56-58, 61 and 133 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity, or a polynucleotide sequence that hybridizes under defined stringent conditions (as in claims 1 and 46) to SEQ D NO: 7 and encodes a polypeptide with an amylase activity, isolated host cells comprising the polynucleotide (as in claim 61) and a micro-array comprising said polynucleotide (as in claim 133), does not reasonably provide enablement for any isolated polynucleotide having at least 90% nucleic acid sequence identity with an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity (as in claims 1 and 46) or enzymatically active fragments wherein said polynucleotides encodes polypeptides having an activity comprising hydrolyzing glucosidic bonds and all the catalytic activity features (several distinct activities) as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8 (as in claim 1 (d)) wherein said fragments of SEQ ID NO: 8 inherently has all the catalytic activity features as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], vectors (as in claims 56-58), host cells comprising said polynucleotides (as in claim 61) and a micro-array comprising said polynucleotides (as in claim 133). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 46, 56-58, 61 and 133 are so broad as to encompass any isolated polynucleotide having at least 90% nucleic acid sequence identity with an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity (as in claims 1 and 46) or enzymatically active fragments wherein said polynucleotides encodes polypeptides having an activity comprising hydrolyzing glucosidic bonds and all the catalytic activity features (several distinct activities) as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8 (as in claim 1 (d)) wherein said fragments of SEQ ID NO: 8 inherently has all the catalytic activity features as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], vectors (as in claims 56-58), host cells comprising said polynucleotides (as in claim 61) and a micro-array comprising said polynucleotides (as in claim 133). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides and encoded polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity

requires a knowledge of and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However, in this case the disclosure is limited to an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity, or a polynucleotide sequence that hybridizes under defined stringent conditions (as in claims 1 and 46) to SEQ D NO: 7 and encodes a polypeptide with an amylase activity, isolated host cells comprising the polynucleotide (as in claim 61) and a micro-array comprising said polynucleotide (as in claim 133). It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides and encoding polypeptides that are having at least 90% nucleic acid sequence identity with the nucleic acid sequence of SEQ ID NO: 7 or a portion thereof and said polynucleotides encoding a polypeptide having an amylase activity comprising hydrolyzing glucosidic bonds and catalytic activity features (several distinct activities) as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above] or a polynucleotide encoding enzymatically active fragment thereof of SEQ ID NO: 8 wherein the fragments inherently possess all the catalytic activity features as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above]. The specification is limited to teaching the use of a polynucleotide sequence of SEQ ID NO: 7 encoding a polypeptide having an amylase activity or a polynucleotide encoding an amino acid sequence of SEQ ID NO: 8, but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make and use the claimed polynucleotides and encoded polypeptides, the lack of guidance,

working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (for example, see Whisstock et al., Prediction of protein function from protein sequence and structure. Q Rev Biophys. 2003, Aug. 36 (3): 307-340. Review), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is not routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any isolated polynucleotide having at least 90% nucleic acid sequence identity with an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity or enzymatically active fragments wherein said polynucleotides encodes polypeptides having an activity comprising hydrolyzing glucosidic bonds and all the catalytic activity features (several distinct activities) as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8 (as in claim 1 (d)) wherein said fragments of SEQ ID NO: 8 inherently has all the catalytic activity features as recited in claim 1(a) to (i), [should read as Claim 1 (a) to

(k), see claim objections above], vectors, host cells comprising said polynucleotides and a micro-array comprising said polynucleotides, as claimed in claims 1, 46, 56-58, 61 and 133, because the specification does not establish: (A) a rational and predictable scheme for modifying specific nucleotides in the polynucleotide sequence of SEQ ID NO: 7 encoding a polypeptide having an amylase activity and said polynucleotide sequences hybridizing under defined stringent conditions and encodes a polypeptide with an amylase activity or enzymatically active fragments wherein said polynucleotides encodes polypeptides having an activity comprising hydrolyzing glucosidic bonds and all the catalytic activity features (several distinct activities) or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8 wherein said fragments of SEQ ID NO: 8 inherently has all the catalytic activity features as recited; (B) a rational and predictable scheme for modifying any nucleic acid residue or an amino acid residue in the encoded polypeptide with an expectation of obtaining the desired biological function i. e., all the recited catalytic features in the claims; (C) the tertiary structure of the molecule and folding patterns that are essential for the desired biological activity and tolerance to modifications; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Furthermore, the art teaches that the different activities such as α-amylase or β-amylase or glucoamylase or exoamylase activities are distinct enzymatic reactions/catalysis and said activities are encompassed in distinct polypeptides encoded by distinct polynucleotides having distinct structures and applicants' have not provided guidance regarding modifying the nucleic acid structure of SEQ ID NO: 7, such that said variant encodes a polypeptide with all the several distinct activities.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides and polypeptides with an enormous number of modifications. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1975)). Without sufficient guidance, determination of polynucleotides and polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 61 (directed to a transformed cell comprising the vector of claim 57 or the nucleic acid of claim 1, wherein the cell is a mammalian cell) is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, because, while claim 61 is enabling for an isolated host cell transformed with the synthetic nucleic acid as claimed, does not reasonably provide enablement for transgenic multi-cellular organisms or host cells within a multi-cellular organism that have been transformed with the synthetic nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claim.

Claim 61 in part is so broad as to encompass transgenic multi-cellular organisms and host cells transformed with specific nucleic acids, including cells in *vitro* culture as well as within any multi-cellular organism. The scope of the claim is not commensurate with the enablement provided by the disclosure with regard to extremely large number of transformed organisms broadly encompassed by the claims. While methods for transforming cells *in vitro* are well

known in the art, methods for successfully transforming cells within complex multi-cellular organisms are not routine and are highly unpredictable. Furthermore, methods for producing a successfully transformed cell within the multi-cellular organism are unlikely to be applicable to transformation of other types of multi-cellular organism as multi-cellular organisms vary widely. However, in this case the disclosure is limited to only host cells *in vitro*. Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the use of host cells within a multi-cellular organism for the production of polypeptide. The scope of claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA)). Without sufficient guidance, expression of genes in a particular host cell and having the desired biological characteristics is unpredictable, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F. 2d 731, 8 USPQ 2nd 1400 (Fed. Cir., 1988). It is suggested that the applicants limit the claim to " An isolated recombinant host cell …".

Written Description

Claims 1, 46, 56-58, 61 and 133 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 46, 56-58, 61 and 133, as interpreted, are directed to a genus of nucleic acids wherein said nucleic acids encompass a large number of variant polynucleotides encoding

polypeptides of any function or several distinct activities; i.e., any isolated polynucleotide having at least 90% nucleic acid sequence identity with an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity or enzymatically active fragments wherein said polynucleotides encodes polypeptides having an activity comprising hydrolyzing glucosidic bonds and all the catalytic activity features (several distinct activities) as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8 (as in claim 1 (d)) wherein said fragments of SEQ ID NO: 8 inherently has all the catalytic activity features as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], vectors, host cells comprising said polynucleotides and a micro-array comprising said polynucleotides. As discussed in the enablement rejection above, the art teaches that the different activities such as α-amylase or β-amylase or glucoamylase or exoamylase activities are distinct enzymatic reactions/catalysis and said activities are encompassed in distinct polypeptides encoded by distinct polynucleotides having distinct structures and applicants' have not provided description of the variants of SEQ ID NO: 7 encoding a polypeptide with all the several distinct activities.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are

representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case, there is no structure associated with functional limitations recited with regard to the members of the genus of polynucleotides claimed in claim 1, 46, 56-58, 61 and 133 (several distinct activities) i.e., a genus of nucleic acids wherein said nucleic acids encompass a large number of variant polynucleotides encoding polypeptides of any function or several distinct activities wherein said isolated polynucleotide having at least 90% nucleic acid sequence identity with an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity and said polynucleotide sequences hybridizing under defined stringent conditions to SEQ ID NO: 7 or enzymatically active fragments wherein said polynucleotides encodes polypeptides having an activity comprising hydrolyzing glucosidic bonds and all the catalytic activity features (several distinct activities) as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8 (as in claim 1 (d)) wherein said fragments of SEQ ID NO: 8 inherently has all the catalytic activity features as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], vectors, host cells and micro-arrays comprising said polynucleotides.

A sufficient written description of a genus of polynucleotides may be achieved by a recitation of a representative number of polynucleotides defined by their nucleotide sequence or a recitation of structure-function correlated features common to members of the genus, which features constitute a substantial portion of the genus. However, in the instant case, the genus of nucleic acids wherein said nucleic acids encompass a large number of variant polynucleotides encoding polypeptides of any function or several distinct activities. While the specification in the

instant application discloses the structure of an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity, or a polynucleotide sequence that hybridizes under defined stringent conditions to SEQ D NO: 7 and encodes a polypeptide with an amylase activity, isolated host cells and micro-array comprising the polynucleotide and said polynucleotide (SEQ ID NO: 7) is not representative of the structure and function of all members of the claimed genus. The specification fails to disclose by any relevant, identifying characteristics or functional properties of all the members of the genus i.e., any information as to the structures associated with functions (several distinct activities) i.e., a genus of nucleic acids wherein said nucleic acids encompass a large number of variant polynucleotides encoding polypeptides of any function or several distinct activities wherein said isolated polynucleotide having at least 90% nucleic acid sequence identity with an isolated polynucleotide of SEQ ID NO: 7 or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8 (as in claim 1 (d)) wherein said fragments of SEQ ID NO: 8 inherently has all the catalytic activity features as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], vectors, host cells comprising said polynucleotides.

The genus of polynucleotides and encoding polypeptides required in the claimed invention is an extremely large structurally and functionally variable genus. While the argument can be made that the recited genus of polynucleotides is adequately described by the disclosure of the structure of an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity, or a polynucleotide sequence that hybridizes under defined stringent conditions and encodes a polypeptide with an amylase activity having an amino acid sequence of SEQ ID NO: 8, since one could use structural homology to isolate those polynucleotide and encoding

polypeptides recited in the claims. As taught by the art, even highly structurally homologous polynucleotides and encoded polypeptides do not necessarily share the same function. For example, Witkowski et al., (Biochemistry 38:11643-11650, 1999), teaches that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al., (J. Bacteriol. 183(8): 2405-2410, 2001), teaches that two naturally occurring *Pseudomonas* enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al., (Science 282:1315-1317, 1998), teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Therefore, the claimed genera of polynucleotides include encoding polypeptides having widely variable structure and associated functions, since minor changes in structure may result in changes affecting function and no additional information correlating structure with several distinct functions has been provided.

Due to the fact that the specification only discloses an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity, or a polynucleotide sequence that hybridizes under defined stringent conditions to SEQ D NO: 7 and encodes a polypeptide with an amylase activity, isolated host cells and a micro-array comprising the polynucleotide, and the lack of description of any additional species/variants/mutants/recombinants by any relevant, identifying characteristics or properties or structure-function correlationship for the cited several distinct functions/activities, one of skill in the art would not recognize from the disclosure that applicant was in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 46, 56-58 and 61 in part are rejected under 35 U.S.C. 102(b) as being anticipated by Hulsmann et al., (J. Bacteriol., 2000, Vol. 182 (22): 6292-6301). Claims 1, 46, 56-58 and 61 in part are directed to any isolated polynucleotide having at least 90% nucleic acid sequence identity with an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity (as in claims 1 and 46) or enzymatically active fragments wherein said polynucleotides encodes polypeptides having an activity comprising hydrolyzing glucosidic bonds and all the catalytic activity features (several distinct activities) as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8 (as in claim 1 (d)) wherein said fragments of SEQ ID NO: 8 inherently has all the catalytic activity features as recited in claim 1(a) to (i), [should read as Claim 1 (a) to (k), see claim objections above], vectors (as in claims 56-58), host cells comprising said polynucleotides (as in claim 61). Hulsmann et al., disclose the complete cloning, sequencing and isolation of a polynucleotide sequence having 100% sequence identity to SEQ ID NO: 7 of the instant application, said polynucleotide sequence annotated as maltose transport system of *A.acidocaldarius* encodes six

genes encoding open reading frames for transport components, including maltose binding protein, and two starch-degrading enzymes i.e., *cdaA* (cyclomaltodextrinase) and *glcA* (alpha-gluocosidase; 1, 4-α-D-glucan glucohydrolase activity) having the activity of hydrolyzing glucosidic bonds in polysaccharides (Abstract section, page 6292; column 1, second paragraph, page 6293; column 2, page 6293, Gene Cloning and Construction of Plasmids; see also sequence alignments provided). The *glcA* (alpha-gluocosidase) polypeptide of said reference has 93.1% sequence homology and a 100% best local similarity to SEQ ID NO: 8 or enzymatically active fragment thereof of the instant application (as in claim 1(d); see sequence alignment provided), claim 1(d) as written does not assign a specific enzymatic activity and therefore examiner takes the position that the reference polypeptide having alpha-gluocosidase activity meets the limitation of claim 1(d) i.e., a polypeptide having a sequence of SEQ D NO: 8 or enzymatically active fragments thereof. Therefore, the reference of Hulsmann et al., (J. Bacteriol., 2000, Vol. 182 (22): 6292-6301) anticipate claims 1, 46, 56-58 and 61 in part of the present invention.

Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 46, 56-58 and 61 in part are rejected under 35 U.S.C. 103(a) as being unpatentable over Hulsmann et al., (J. Bacteriol., 2000, Vol. 182 (22): 6292-6301). The teachings of Hulsmann et al., are described above (see 102 (b) rejection). Although Hulsmann et al., teach the complete cloning, sequencing and isolation of a polynucleotide sequence having 100% sequence identity to SEQ ID NO: 7 of the instant application, said polynucleotide sequence annotated as maltose transport system of *A.acidocaldarius* encodes six genes encoding open reading frames for transport components, including maltose binding protein, and two starch-degrading enzymes i.e., *cdaA* (cyclomaltodextrinase) and *glcA* (alpha-gluocosidase), said alpha gluocosidase having the activity of hydrolyzing glucosidic bonds in polysaccharides (Abstract section, page 6292; column 1, second paragraph, page 6293; column 2, page 6293 Gene Cloning and Construction of plasmids; see also sequence alignments provided), said reference is silent regarding said nucleic acid further comprising a sequence encoding a heterologous polypeptide sequence (as in claim 1 (f) to (i), [should read as (h) to (k); see claim objections above]). The many advantages of recombinant production of useful proteins are well known within the art (for example, see Chapters 1-3, 16 and Vectors-Appendix 5 in Current Protocols in Molecular Biology, Ed., Ausubel et al., Published by John Wiley and Sons, New York, NY, USA, 1990), as are recombinant methods of obtaining the necessary genes. These advantages include a) the ability to produce much larger quantities of the protein cloned into suitable expression vectors, b) being able to produce the protein in more easily handled organisms (host cells), c) construction of fusion proteins with suitable tags/heterologous polypeptides for easy detection and purification of expressed proteins, d) appropriate targeting of expressed polypeptides to the sub-cellular compartment of interest in the host cell of interest by expressing said polypeptide as a fusion

protein comprising heterologous signals such as leader sequences, e) for reducing the number of steps necessary for the purification of a protein and f) producing the protein in a purer form by using an organism that does not include naturally occurring contaminants of the protein. As such disclosure of a polynucleotide encoding a useful polypeptide such as that of Hulsmann et al., clearly suggests to a skilled artisan to produce large quantities of the said protein comprising appropriate heterologous sequences such as tags, epitopes or leader sequences depending on the experimental need. Therefore, it would have been obvious to one of ordinary skill in the art to isolate and express any isolated polynucleotide having at least 90% nucleic acid sequence identity with an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an amylase activity or enzymatically active fragments wherein said polynucleotides encodes polypeptides having an activity comprising hydrolyzing glucosidic bonds and all the catalytic activity features (several distinct activities), or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8, vectors, host cells comprising said polynucleotides and as disclosed by Hulsmann et al., using well known recombinant methods for the isolation of such genes, insertion of the isolated gene into a suitable expression vector comprising a nucleic acid encoding a heterologous polypeptide (as in claim 1 (f) to (i), [should read as (h) to (k); see claim objections above]), introducing said vector comprising said nucleic acids into suitable host cells for a method of producing said polypeptides (as in claims 46, 56-58 and 61).

Claims 1, 46, 56-58, 61 and 133 in part are rejected under 35 U.S.C. 103(a) as being unpatentable over Hulsmann et al., (J. Bacteriol., 2000, Vol. 182 (22): 6292-6301) and in view of Brown et al., (Nature Genetics, 1999, Vol. 21: 33-37). The teachings of Hulsmann et al., are

described above (see 102 (b) rejection). Although Hulsmann et al., teach the complete cloning, sequencing and isolation of a polynucleotide sequence having 100% sequence identity to SEQ ID NO: 7 of the instant application, said polynucleotide sequence annotated as maltose transport system of *A.acidocaldarius* encodes six genes encoding open reading frames for transport components, including maltose binding protein, and two starch-degrading enzymes i.e., *cdaA* (cyclomaltodextrinase) and *glcA* (alpha-gluocosidase), said alpha gluocosidase having the activity of hydrolyzing glucosidic bonds in polysaccharides (Abstract section, page 6292; column 1, second paragraph, page 6293; column 2, page 6293 Gene Cloning and Construction of plasmids; see also sequence alignments provided), said reference is silent regarding an array i.e., said polynucleotide immobilized on a suitable matrix. Brown et al., teach the use of DNA micro-arrays as a vehicle for exploration for carrying out genome-wide surveys of gene expression patterns or functions that involves arraying discrete genes of interest (polynucleotide sequences) immobilized on a suitable matrix (Abstract section and entire document). It would have been obvious to a person of ordinary skill in the art to combine the teachings of Hulsmann et al., and Brown et al., to produce an array comprising the polynucleotide sequence of SEQ D NO: 7 and motivation to do so derives from the use of DNA micro-arrays for exploring at a molecular level, expression, function and the occurrence of polynucleotide sequences having homology to SEQ ID NO: 7 in other organisms i.e., genome-wide surveys of gene expression patterns or functions with DNA-micro-arrays (Brown et al.,). The expectation of success is high for producing an array comprising the immobilized sequence of SEQ ID NO: 7, because Hulsmann et al., teach the complete cloning, sequencing and isolation of a polynucleotide sequence having 100% sequence identity to SEQ ID NO: 7 of the instant application and Brown et al., teach the use of

DNA micro-arrays as a vehicle for exploration for carrying out genome-wide surveys of gene expression patterns or functions, that involves arraying discrete genes of interest (polynucleotide sequences) immobilized on a suitable matrix. Therefore, claims 1, 46, 56-58, 61 in part and 133 in part are rejected under 35 U.S.C. 103(a) as being unpatentable over Hulsmann et al., (J. Bacteriol., 2000, Vol. 182 (22): 6292-6301) and in view of Brown et al., (Nature Genetics, 1999, Vol. 21: 33-37).

Allowable Subject Matter/Conclusion

None of the claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ganapathirama Raghu/
Patent Examiner
Art Unit 1652
May 10, 2008.